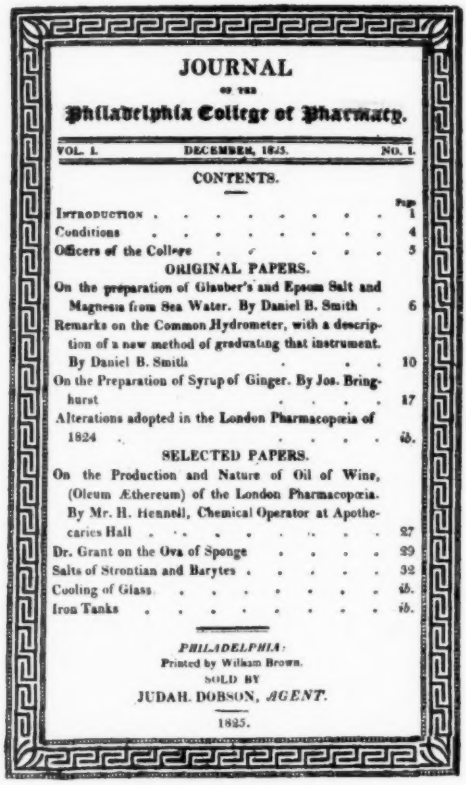
American Journal of Pharmacy

AND THE SCIENCES SUPPORTING PUBLIC HEALTH



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CONTENTS.

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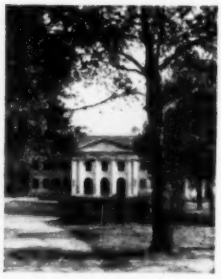

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AMERICAN JOURNAL OF PHARMACY

AND THE SCIENCES SUPPORTING PUBLIC HEALTH

Since 1825

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CONTENTS

EDITORIAL

INFORMATION FOR THE PHARMACIST

THE official statement by the Food and Drug Administration to the effect that information concerning prescription products may accompany the package paves the way for a change that will be a great service to the pharmacist.

For many years it has been established that the pharmacist assumes the major responsibility for the saftey of drugs prescribed by the physician, indeed this has been the decision in many legal cases. Not only must the pharmacist exercise judgment concerning the method or route by which the drug is to be used but he also must make certain that the dosage prescribed is reasonably safe.

The number of prescription specialities today is almost unbelievable, and the amount of information which the pharmacist is presumed to have at his instant command is encyclopedic in volume. Official drugs constitute a minority of prescriptions today, and consequently, the pharmacist is faced with the necessity of keeping reasonably well informed on the thousands of proprietaries—no small task, if at all possible. The average physician is not in as difficult a position. He usually picks some forty or fifty products in which he has confidence and prescribes them with fair regularity. Occasionally, he goes outside this list for the treatment of some unusual patient, but this is an exception. There are, of course, those physicians who prescribe, at least once, every new proprietary that is discussed with them by a detail man. Many of these practitioners never gain sufficient experience with most of these products to understand them, and their use of drugs is nothing short of empiric. It is fortunate that pharmacists are there to check on the hazards that this engenders.

For a number of years the pharmacist has had to resort to all kinds of devices to keep posted on the essential data concerning the drugs which he was dispensing. Unfortunately, not all manufacturers are sympathetic with his problem, and they have not always done all that might have been done to help. Many pharmacists, themselves, by their attitude have discouraged manufacturers from helping them meet this problem. The sullen and suspicious attitude that some pharmacists exhibit toward manufacturers rarely is justified, and it is an example of lack of cooperation in which both parties suffer.

The inclusion of information concerning a prescription product in the package supplied the pharmacist should prove a real step forward and one that should help the pharmacist meet his professional obligations, both in checking on the orders of the physician and safeguarding the public. Manufacturers who take immediate advantage of this clarification by the F. D. A. will do much to earn the good-will of the practicing pharmacist.

One other very important direction in which manufacturers might easily cooperate to help the pharmacist has been stated repeatedly by many others. The initial suggestion, we believe, was made several years ago by one of our Canadian colleagues. It is of such importance that it was adopted as a formal resolution by the House of Delegates of the American Pharmaceutical Association at its last convention held in Jacksonville, Florida. This resolution follows:

> Resolved, that we recommend to manufacturers that they devise a uniform card suitable for filing by the retail drugstore and distribute such cards to the drugstores, including the followings facts: Name of all new products; name of manufacturers; preparation; use; dose and contraindications.

The Council of the American Pharmaceutical Association instructed the Secretary to refer the substance of this resolution to the appropriate organizations.

We should like to add our own indorsement to this resolution. The adoption of a uniform index card supplying these essential data would be extremely helpful to the pharmacist. At the present time data supplied by many manufacturers comes in such a heterogeneous nondescript form that it defies systematic filing. A few companies have adopted a uniform system for their own products, but it cannot be integrated with that of another company. Many pharmacists feel constrained to buy expensive books giving nothing but manufacturers' data collected in a useful form.

Surely competition between companies is not such that this small area of agreement and cooperation is impossible. We urge the American Drug Manufacturers' Association and the American Pharmaceutical Manufacturers' Association to give this matter their joint attention and not let some few who may oppose this program obstruct its purposeful execution.

L. F. Tice

CURRENT TRENDS IN MODERN MEDICINALS

By Madeline O. Holland, D. Sc.*

(Part II)

EDITOR'S NOTE: *This month we present the last part of a comprehensive review of pharmaceutical progress. Part I appeared in the November number.*

DIAGNOSTIC AIDS

In some diseases diagnosis is based only on the symptoms and appearance of the patient. In others there are available tests, which, although in some cases not conclusive, at least point the way to the proper diagnosis. A number of such diagnostic tests have been developed in the past year.

Blood Protein

Two drops of blood and a minimum of equipment are all that are necessary to perform a simple, quick test which is an aid in diagnosing liver diseases, tuberculosis and other conditions. It is based upon the amount of individual plasma proteins in the blood. The blood drops are first mixed with a solution of sodium sulfate and then poured into a glass tube packed with diatomaceous earth. By pouring the sodium sulfate solution through the tube the albumin of the blood is removed. The other plasma proteins are then removed separately by washing with different salt solutions. The quantity of each protein present can then be determined by the amount of ultraviolet light absorbed when they are exposed to these rays. Cirrhosis, cancer of the liver and tuberculosis disturb the blood protein balance which can be determined. Tuberculosis or other lung disorders will be evidenced by a high content of fibrinogen.

* Managing Editor, *American Professional Pharmacist;* Technical Editor, *Medical Times.*

Cancer Test With Infra-Red

At present there is no simple self-test for the early detection of cancer as there is for diabetes. However, considerable research has been directed toward this goal with the result that new and more simplified tests, although not for use by the individual, have been devised. In the meantime tissue smears, determination of sedimentation rate and occult blood together with gastric analysis are still useful in confirming the diagnosis. Only recently it was reported by the Sloan-Kettering Institute for Cancer Research that, through use of new technics involving the obtaining of so-called "fingerprints" of hormone substances by means of infra-red light, it was possible to obtain the print of a strange hormone that shows up in most cancer cases—either before detection of the disease or during the course of the disease. It is believed that this derivative comes from the adrenal glands. It was demonstrated in the excretions of 9 out of 10 cases of cancer of the prostate, 4 out of 4 of cancer of the larynx, 2 of 2 cases of breast cancer, 1 of 1 case of cervical cancer and 4 of 4 lymphatic leukemia patients.

Cancer Test (D-S-B)

One of the most recently developed tests for which the materials have been made available commercially is that for determining the reducing power of plasma. It has been found that the plasma of patients with cancer generally requires a longer time to decolorize a solution of methylene blue than does the plasma from patients free of malignancy. Exceptions are found in those persons afflicted with tuberculosis, active rheumatic fever, pregnancy, and possibly those with cirrhosis of the liver and those receiving penicillin. A second test with brilliant cresyl blue is used on borderline diagnoses. It has been found that adequate therapy reversed the characteristic alternations in reducing power. The two solutions can therefore be used to follow response to treatment as well as to diagnostic tests. Known as D-S-B this diagnostic aid is supplied by Endo Products Inc. and consists of two dye solutions designated as BMS (methylene blue) and BCS (brilliant cresyl blue), standardized for their reducing power on human plasma.

Cancer Test With Gelfoam

A tumor diagnosis kit recently was developed from the studies of Dr. A. Gladstone to facilitate diagnosis of cancer in accessible regions of the body, such as lesions of the skin, mouth, bronchi, lower bowel, cervix and uterus. Each kit contains two sterile biopsy swabs and one 30 cc. bottle of fixative solution (Formaldehyde Solution, U. S. P., 1:10). A mailing carton and gummed address label are furnished to facilitate shipment of the specimen to the pathologist. The label of the formaldehyde solution vial and the package insert provide space for pertinent information concerning the swab material and the history of the patient from whom the biopsy material was taken. In the Gladstone sponge biopsy technique the swab is clamped along one margin by a surgical sponge forceps. The ulcer is wiped clean with dry, sterile gauze and then the dry sponge is rubbed gently over the area. After the sponge becomes wet, it is pressed more firmly against the lesion with slight rubbing. The cells from the area will adhere to the sponge surface. The sponge is then placed in the formaldehyde fixing solution and sent to the laboratory where it is subjected to routine tissue sectioning technique. The cells adhering to the swab may then be examined microscopically and identified. The swabs are made of Gelfoam, the new gelatin sponge, and the kit is marketed by The Upjohn Co. as Gelfoam Tumor Diagnosis Kit.

Cancer and Serum Proteins

Huggins and his colleagues have been investigating the relationship of serum proteins to human cancer. They have found that frequently these proteins are deficient in quantity and abnormal in kind. The qualitative abnormalities cannot be defined in a precise fashion, but they can be recognized as present when the serum proteins are subjected to heat, because of the defective coagulation. Although this is not specific as a diagnostic instrument, it is useful in helping to confirm the diagnosis. Unfortunately there are false positive reactions in this test which may make it difficult to interpret. Serum from pulmonary tuberculosis and cancer patients coagulates in much the same characteristic manner and serum from patients with benign tumors coagulates in the normal manner.

Cancer appears to produce a defect in the coagulative capacity of the serum proteins with respect to those linkages available for coagulation when the serum is heated. It was first necessary to determine the smallest amount of protein which would undergo coagulation.

Because iodoacetate inhibits clotting of serum proteins, this substance was used to develop an index which relates the inhibition of clotting by iodoacetate to the quantity of protein present in serum and, therefore, to the total availability of those linkages necessary for coagulation. In these tests it was found that patients with cancer had a lower index than normal patients. However, there were some patients with non-malignant but, nevertheless, serious diseases who also showed low indices. This defect in coagulation was not observed in normal pregnancy, in new-born infants, or in non-pulmonary tuberculosis.

Because these tests are still highly experimental, they will not be considered in great detail at this time. However, it is possible that future investigations and further improvements may make them of great value in the diagnosis of cancer and other serious diseases.

Cancer and Enzyme Inhibitors

Very recently it was announced that a simple, quick and inexpensive method for measuring the effect of therapy on cancerous tissue had been developed. This procedure is based on an analysis of blood components. Not only can it be used to determine whether a new treatment will be effective, but also it can be used to show the progress of individual patients.

There are present in the blood two enzyme inhibitors which prevent the enzymes from doing too much work, for example, when they break down not only food but also the digestive tract tissues. The two enzymes which are inhibited are rennin, a milk-curdling enzyme in the stomach, and chymotrypsin, a milk-digesting enzyme in the pancreas. Presence of the inhibitors of the two enzymes is indicative that cancer is present somewhere in the body. When the cancer is actively growing, analysis will reveal that more of the chymotrypsin inhibitor is present than of the rennin inhibitor. As the cancer growth diminishes the quantity of rennin inhibitor increases and the quantity of chymotrypsin inhibitor decreases. The changes

in the ratio of these two substances can be determined by successive tests. Thus, from the changing ratio the developments in a cancer patient can be measured. This test is believed to be applicable to all of the standard forms of cancer such as tissue growths and also in leukemia.

It can be completed in 24 hours and can be performed by trained laboratory technicians. In the past the only means of testing for the progress of a cancer or for the progress of treatment has involved a considerable period of time, and in many instances an operation was necessary if the cancer was internal. Death of the patient frequently was the only sign that the cancer had renewed its activity. Generally, 5 years is allowed to lapse before it can be stated definitely that a cancer has been arrested in its growth. This test of enzyme inhibitors, like other tests, is not conclusive in conditions such as pregnancy, tuberculosis and similar infections, and after surgery where there is extensive tissue growth. However, since the presence of these conditions is obvious, erroneous diagnosis is generally not likely.

It is suggested that this test may be applied more extensively in checking tissue biopsies which are used to determine the severity of the malignancy. In determining the effectiveness of therapy it has shown considerable differences in the efficiency of X-ray in various cases of breast cancer. Some workers have hopes that use of this test may accelerate the development of proper therapy, because it is now possible to determine whether the right procedure for the individual case is being followed.

Coccidioidin

Coccidioidomycosis is a disease of the lungs caused by *Coccidioides immitis,* and in its initial stage resembles pulmonary tuberculosis. For this reason it is not always diagnosed properly. Recently there has been made available a filtrate extract which can be used for skin testing in a fashion similar to intradermal tuberculin. Known as Coccidioidin 1:100 this diagnostic aid is available from Cutter Laboratories.

Hogben-Frog Test for Pregnancy

Although some have used the unconcentrated urine in this frog test, it may result in the frog's death, so it is preferable to use a powder prepared by acetone precipitation from 80 cc. of a morning

urine specimen. The powder is taken up in 2 cc. of water, and the whole injected into the dorsal lymph space. Examination of the animals in 6 to 12 hours will show the extrusion of a large number of eggs into the water of the tank, if the test is positive. This test is 98 to 99 per cent accurate. Recently it was found that the male North American frog, *Rana pipiens,* could be used for determining pregnancy. Some workers prefer to inject 5 cc. of the filtered morning urine into the dorsal lymph sac, whereas others believe that 1 cc. of a concentrated form made from 100 cc. of morning urine should be used. After 1/2 hour the frog is grasped firmly in the left hand, and the right leg held between the operator's thumb and second finger. The left leg is then held between the thumb and index of the right hand, and the leg drawn up to the frog's side. The cloaca is then touched to a clean glass slide so that some of the cloacal fluid is obtained. This is examined for the presence of sperm cells which indicate a positive result. The test not only is 99 per cent accurate, but it is also inexpensive; the animal is easily available; and the time interval involved is short. The frog should be discarded after use because it may give a false-negative test after a positive test.

Two-hour Rat Test for Pregnancy

The test believed to have the greatest accuracy is the two-hour rat test using immature, female rats, 21 to 55 days old and weighing 30 to 80 Gm. A dose of 2 cc. of unconcentrated urine, not necessarily a morning specimen, is injected intraperitoneally into the lower right and left abdominal quadrants. After two hours the rat is asphyxiated with ether (other agents may produce false positive readings). The viscera are exposed without loss of blood and the ovary examined with as little trauma as possible to the surrounding tissues. A positive result is indicated by ovarian hyperemia. However, a positive reading cannot be expected unless the test is performed at least 1 week to 10 days after the missed menstrual period or 21 to 35 days after conception has taken place. This is true of the other urine tests also. The test is 99.5 per cent accurate, excluding cases of ectopic pregnancy. The test animals are readily available, and their age and weight can vary considerably, in contrast to the close specifications of the other tests. The urine is easily administered, and the test can be performed in 2 to 3 minutes. The endpoint is easy to read and does not require a great deal of experience for ac-

curacy. The patient is not inconvenienced or made uncomfortable in the collection of the specimen. The urine does not have to be purified, concentrated or its pH changed. A morning specimen is preferable but not absolutely necessary.

All of these tests, of course, are based upon the presence of gonadotrophic hormones which are characteristically present in urine during pregnancy. False positive reactions may be observed if gonadotrophins or certain other hormones are being given to the patient or if there are rare tumors of the ovary, pituitary or adrenal cortex present.

Plastotest

Dr. H. J. Corpor has developed a new test for tuberculosis which should be of value in mass testing. It is quicker than the patch test and does not irritate the skin as the latter does. It is considered to be 80 to 85 per cent accurate. The testing material is composed of a new tuberculin in a quick-drying base. It is applied to the skin, allowed to dry, and after 24 hours it is peeled or washed off. A positive test is indicated by redness and small blisters. Known as Plastotest this material resembles nail polish in its texture.

Pectin Paste

A patent has been issued within the past year for a new pectin paste as an x-ray contrast medium. The compound consists of a paste of pectin, glycerin, benzoic acid, and a physiological salt solution, mixed with barium sulfate. It is stated that this paste produces no clinical after-effects or side reactions, is soothing and non-irritating to mucosal tissues, contains no irritating gums or resins, and is miscible with the contents of the digestive tract without affecting its chemistry. It is anti-fermentative, more adherent to the rugae of the intestinal tract and gastro-enteric mucosa, and insures even distribution of barium. The new medium is in fine, evenly-dispersed suspension and insures an even flow through the intestinal tract without sagging or pocketing of barium salts in the loops of the intestines or in the rugae of the intestinal tract.

Secretin

A hormone elaborated by the mucosa of the small intestine, is useful in diagnosis of pancreatic dysfunction and biliary disease. The first American Secretin, it has been made available commercially by Wyeth, Inc.

VDRL Antigen

Syphilis is a disease which is sometimes difficult to diagnose because malaria and other conditions tend to produce false positive reactions. Consequently, considerable research has been devoted to a search for an antigen which would be specific. Recently the Venereal Disease Research Laboratories of the United States Public Health Service announced the development of an improved antigen. It consists of an alcoholic solution containing cardiolipin 0.03 per cent, cholesterol 0.09 per cent and a sufficient quantity of lecithin to produce standard reactivity. It may be employed in either a slide or tube test, with serum and spinal fluid, and is adapted for use in large scale surveys. It is wholly effective in detecting syphilis in the presence of malaria and other conditions and has been recognized officially by many major cities as an acceptable blood test for marriage licenses and food handler's certificates. Many large industrial organizations are using the antigen in pre-employment examinations. Lederle Laboratories Division of American Cyanamid Co. are making this available under the name V. D. R. L. Antigen, the name derived from the initials of the laboratories in which it was developed.

DIURETIC

Mercuhydrin, Oral

The mercurial diuretics have been employed for many years to control edema in cardiac therapy. However, those available have always required parenteral administration. Recently there has been made available tablets of sodium methoxymercuripropylsuccinylurea with theophylline and ascorbic acid for oral administration. Although these tablets may be used alone in some instances for maintenance therapy, they generally will serve best as a supplement to parenteral administration. In conjunction with parenteral administration, the new oral product permits reduction in the number of injections and longer intervals between treatments. For the ambulant cardiac, oral diuretic therapy is of decided advantage to both the patient and the physician. Its use facilitates the frequent dosage schedules of modern diuretic therapy. Addition of the ascorbic acid increases the tolerance to and potentiates the action of the mercurial. This new oral product is known as Mercuhydrin With Ascorbic Acid and is marketed by Lakeside Laboratories, Inc.

DRUGS USED FOR EFFECTS ON HIGHER NERVE CENTERS

Paradione

Epilepsy is a condition for whose therapy a number of drugs have been developed; these drugs have achieved varying degrees of success in treatment. Some few years ago a new synthetic drug, trimethadione (3,5,5-trimethyloxazolidine-2,4-dione), was announced and produced startling results in the control of petit mal, myoclonic and akinetic epilepsy. It appeared to have considerable advantage in many cases over the existing methods of therapy. Recently a homolog of this compound, paramethadione, has been made available. It differs only in the substitution of an ethyl for a methyl group on carbon 5. The drug is an oily liquid, slightly soluble in water, but quite soluble in alcohol. It has the same indications as trimethadione. Some patients whose seizures are not controlled by the trimethadione can be improved with paramethadione, and vice versa. Like its homolog, the new drug is contraindicated in patients with severe renal or hepatic disorders. The dosage is based on the response of each patient. For older children and adults the initial dose is 0.9 Gm. daily in divided doses. The amount should be increased or decreased according to the response or the occurrence of undesired side-effects. Side-effects resulting from paramethadione therapy appear to be fewer in number and less severe than those accompanying trimethadione administration. Photophobia, the most frequent reaction to trimethadione, is infrequent with the new drug. Known as Paradione the new homolog of Tridione is available from Abbott Laboratories.

DRUGS USED IN THE TREATMENT OF CANCER AND LEUKEMIA

Aminopterin

The pteroyl glutamic acid compounds have been studied for several years for their possible effects in cancer and leukemia. Several of these derivatives were described in last year's review. Further investigations still are being conducted to determine their effectiveness. Recently considerable attention has been focused on another drug (N-[p-(2,4-diamino-6-pteridylmethylamino)benzoyl] glutamic acid) developed by Lederle Laboratories. Known as

Aminopterin, it is under clinical trial. Although not a cure for leukemia, it does slow down the disease, particularly in children, and allows them to lead a fairly normal life, provided periodic treatments are continued. It is believed to be the first drug to really arrest this cancer of the bloodstream.

Testosterone

Use of the male horomone, testosterone propionate, in large doses has been found to affect, in a striking manner, cancer of the female breast. In some cases the primary lesion and the soft part metastases regress. Osseous metastasis increases in calcification, and pain disappears concurrently with osteoblastic changes. Although there are no toxic effects, a certain degree of masculinization may develop. The dosage given is 50 mg. daily or 100 mg. on alternate days for a total weekly dosage of 300 mg. Testosterone propionate is available from several pharmaceutical firms.

EQUIPMENT

New Mortar and Pestle

The conventional types of mortars and pestles which are employed by pharmacists today have been in use for many centuries. Not only have they found application in Pharmacy but in many other fields as well, and they have proved to be very useful and effective. However, progress very often necessitatates changes. The trituration of prescription ingredients in the conventional type of mortar and pestle is rather slow and tedious. By changing the basic design in some fashion, it was thought that this procedure might be accomplished faster and more efficiently. As a consequence, a flat-bottom mortar and a flat-bottom pestle, both with vertical sides, were designed. The mortar and pestle were then made according to this design, and the vertical sides of the pestle were made to correspond to those of the mortar. After several trials it was found that the pestle must be held in a vertical position and moved in an outward rotary pattern to be certain of complete trituration. This differs considerably from the type of motion used to triturate in the mortars now used. Use of this mortar does not necessitate scraping the sides with the spatula as frequently as with the conventional type.

The effectiveness of this new type of mortar and pestle is striking. Because the diameter of the pestle is approximately of the same

dimension as the radius of the mortar the crushing, grinding and distributing surfaces are increased. A preliminary test with charcoal and heavy magnesium oxide was first made. The 2 types of mortars and pestles were used, and into each mortar was placed 1 dram of heavy magnesium oxide. Three grains of charcoal were sprinkled over the top, and in each case the pestle was moved in 12 complete revolutions. In the conventional type of mortar and pestle the charcoal appeared as black streaks in the white magnesium oxide, whereas in the new type there was a well-mixed gray powder with no black streaks. Chemical analysis was not done because it was thought that the physical appearance was sufficiently conclusive. Less effort was necessary with this new mortar and pestle in crushing tablets, and the process was more thorough. Grinding and mixing tests also were made and showed considerable improvement in results over the old type of mortar and pestle.

Emulsification is another process which is accomplished more readily and efficiently with the new type of mortar and pestle. A primary emulsion which will not break or crack when diluted 64 times can be prepared in 20 seconds, but 3 minutes of trituration in the conventional type does not produce complete emulsification. Tests with emulsions of heavy mineral oil, acacia and water were made, and photomicrographs revealed that the particle size of the emulsion made in the new type mortar and pestle was considerably smaller and more uniform than that made in the conventional type. Prescriptions containing four ingredients such as acetylsalicylic acid, acetophenetidin, codeine sulfate and belladonna extract have always presented difficulties in trituration. However, with the new type of mortar and pestle the four ingredients can be placed in it together, and a smooth mixture is made with much less effort than previously. This new type of mortar and pestle should be of value to the pharmacist to save both time and effort. It is available from Armstrong Cork Co., Pharmaceutical Division and was designed by a pharmacist, M. L. Cooper of Baltimore, Md.

HORMONES

Although several new developments in the hormone field have been considered elsewhere, there are a few specific developments which can be grouped under this heading.

Buccal Tablets

A new type of tablet has provided a new means of administration of hormones such as testosterone propionate, progesterone, estradiol and desoxycorticosterone acetate. Incorporated in Polyhydrol, a solid solvent for steroid hormones, it is possible to obtain, with these hormones orally, the same effects as obtained from intramuscular injections. They owe their effectiveness to the fact that the hormone is absorbed into the systemic circulation through the buccal and sub-lingual mucosae, by-passing the liver and the portal circulation. They are for use in the same conditions as the parenteral dosage forms. The tablet is placed well into the lower space, adjacent to the buccal surface of the gums, opposite the first molar tooth. It is absorbed in 30 to 60 minutes. Once placed, the tablet should not be disturbed with the tip of the tongue. Eating or drinking is restricted until complete absorption of the tablet has occurred. However, the patient may talk or swallow *ad libitum*. These tablets do not stimulate salivation. Mid-morning, mid-afternoon and before retiring are the best times for administration of this medication.

Buccal tablets of Oreton (testosterone propionate), Proluton (progesterone), Progynon (estradiol) and Cortate (desoxycorticosterone acetate) are available from Schering Corporation. The water soluble hormones are available in ordinary tablet bases for buccal or sublingual adminstration such as Metandren Linguets (Ciba), Linguasorbs Testosterone (Ayerst, McKenna and Harrison), Testosterone Propionate Buccal Tablets (Lilly and Ciba) and Hypoglossals Testosterone (Carnrick).

Pituitary

In January of 1949 it was announced that the recently purified adreno-corticotrophic hormone produced by the pituitary gland possessed a marked growth-inhibiting action. No immediate application of this property to human medicine was possible at the time, but it was found that the hormone possessed important effects on the lymphoid system which is responsible for producing some of the white blood cells. Administration of the hormone to rats resulted in an almost complete disappearance of one organ in the lymphoid system, the thymus, and marked degeneration of the entire system.

Although the hormone itself is not a growth inhibitor, it stimulates the adrenal glands to secrete other hormones which are directly responsible for retarding growth, according to Dr. B. L. Baker of the University of Michigan School of Medicine. Although not applicable at present to human medicine these studies are of value in increasing the understanding of how the body controls growth. Further work is being conducted to learn how and if the pituitary gland, acting through the adrenal gland, may play a part in the control of cancer, a disease characterized by the abnormal growth of body cells. The pure hormone was first isolated by Dr. C. H. Li of the University of California. Dr. Baker had as his collaborator Dr. D. J. Ingle of the Upjohn Research Laboratories.

In later months experiments with another growth hormone isolated in 1944 were revealed by Drs. H. M. Evans and H. Becks of the University of California. This hormone, also from the pituitary gland, has been found to produce giant rats that remained young even though they had reached an age equivalent to 100 for humans. Studies of the organs revealed that the liver, stomach, intestines, kidneys and heart were big but of the right proportions, body size and weight considered. However, the reproductive organs had decreased in size, and the adrenals and the pituitaries had increased in weight, but not in proportion to the gain in bodily weight. Certain of the bone formations were characteristic of acromegaly.

Still more recently a new method of treating gigantism and acromegaly was reported by Drs. L. W. Kinsell, G. D. Michaels, C. H. Li and W. E. Larsen at the University of California Medical School. Although the growth hormone of the pituitary gland is solely responsible for growth in childhood, the steroids or sex hormones from the gonads and the adrenal cortex are responsible from puberty on. These steroids, at the same time, suppress the action of the growth hormone. If the steroids fail to suppress growth, the hormone output in puberty and in adolescence proceeds. Acromegalic gigantism is the result. If normal puberty and adolescence are followed by an overactive pituitary condition, growth may persist after maturity and result in acromegaly. Used both in diagnosis and for determining the effectiveness of therapy is the fact that there is an increase in the amount of inorganic phosphorus in the blood of acromegalics and of pre-pubertal children but not in normal adoles-

cents or adults. A drop in the phosphorus level in an acromegalic patient is an indication that treatment is effective. This test is verified by the fact that there is a corresponding rise in the amount of pituitary growth hormone in the blood in untreated acromegalics and a drop when effective treatment is given. Although not so certain as the phosphorus test it is promising.

Because of these findings the California workers began therapy of 2 female patients having acromegaly with testosterone propionate and ethinyl estradiol. Improvement resulted, and the phosphorus and pituitary-growth hormone levels in the blood dropped. Thus another use for the sex hormones is possible.

Still another pituitary hormone has been isolated by Dr. Li. known as FSH or the follicle stimulating hormone it is believed to play a key role in both male and female fertility. This hormone is believed to stimulate the growth of the ovarian follicles, making possible ovulation, the discharge of the egg out of which, after fertilization, the new life develops. In the male it is believed to stimulate the glands which produce the sperm. This discovery will open the way for more detailed studies of the reproductive cycle and for new research into the physiology of reproduction.

Several new hormone products have been made available in the past year, but only a few employ a new principle.

MOTION SICKNESS

Dramamine

The value of many drugs in the therapy of certain conditions is often discovered accidentally. Such is the case with a new drug, β-dimethylaminoethyl benzohydryl ether 8-chlorotheophyllinate. In 1947 this drug was presented to the Allergy Clinic of the Johns Hopkins Hospital and University to be tested for its value as an antihistaminic in the therapy of hay fever and urticaria. One of the first patients to be given the drug was a pregnant woman who not only had urticaria but also had suffered from carsickness her entire life. It was found that this drug not only relieved the urticaria but also the carsickness, and after further study an investigation of the drug's effect on seasickness was begun. With the cooperation of the Chief of Staff and the Surgeon General of the United States Army a study was begun on a group of the 1,366 soldiers aboard the

United States Army Transport "General Ballou." It was found that the drug not only prevented seasickness in those to whom it was given at sailing time, but that it also relieved the seasickness after the symptoms had developed even in the severest cases. Further studies have shown this drug to be of value also in airsickness and other types of motion sickness.

A very recent report from the Mayo Clinic has stated that this drug also has value in an entirely different field as well. Patients who undergo X-ray or radium treatments for cancer or leukemia frequently develop radiation sickness, which is characterized by nausea, loss of appetite, weakness, exhaustion or prostration. The drug was given to 82 patients who suffered marked nausea after riadiation therapy, and in 65 good to excellent relief was obtained. It was given both before and after therapy.

Thus a drug which started out as an antihistaminic is proving to be useful in various fields of therapy. Known as Dramamine it is marketed by G. D. Searle and Co., Inc.

Mosidal

Another drug which exerts a protective and therapeutic action against motion sickness in human beings, without undesirable side-effects is ethyl-β-methylallylthiobarbituric acid. The best results are obtained when it is started 24 hours before exposure to motion. A dose of 0.15 Gm. (2½ grs.) is taken immediately after breakfast and a second dose of 0.15 Gm. immediately after the evening meal. Absorption of the drug is prolonged when it is taken with a meal. The total daily dose should not exceed 0.45 Gm. Duration of protection after the drug has been discontinued is 15 to 18 hours. Treatment should not be continued for more than five days at a time, and impaired liver function is a contraindication. This drug is available under the name of Mosidal from Abbott Laboratories.

NEW TECHNIQUES

Acne Therapy

Acne is a disfiguring condition which requires, in many cases, extensive therapy often resulting in scars. The use of dry ice in this type of therapy has been reported. Application of small pieces of dry ice to the pustules for 3 to 5 seconds produces good results.

In those cases where the lesions are numerous a larger piece may be applied to a group. If the proper amount of pressure is applied, the skin between the lesions will not be harmed. After application of the dry ice the lesions blister within a few hours, then dry and shrink, resulting usually in involution with little or no scarring.

Artificial Kidney

Artificial kidneys have been employed for some years in certain types of kidney disease to allow the diseased or injured kidney to rest. But in most cases the artificial kidneys used are so large and cumbersome that their use is difficult. Recently Drs. J. A. Sterling, L. B. Weiss, A. Schneiberg and J. C. Doane and engineers W. and R. Bernard developed a new artificial kidney made up of plastic plates separated by thin sheets of cellophane. Grooves cut into the plastic serve as channels in which the blood flows on one side of the cellophane membrane; a "perfusate" solution of glucose and salt in distilled water flows on the other side. When the two streams run through the apparatus, nitrogenous waste products are transferred from the blood to the perfusate by osmosis. When it is to be used, a tube is inserted into an artery in the left wrist of the patient and connected to the artificial kidney. This is placed below the level of the wrist, and a suction pump is attached to the exit valve to aid the heart in forcing through the blood. The perfusate is pumped through in the same or opposite direction to the flow of blood. After the blood flows through the artificial kidney, it is collected in a flask and returned to the body through a vein in the right wrist. In order to compensate for the temporary removal of fluid a transfusion of plasma or blood is given. In this manner the blood is cleansed, and the patient's kidneys given a rest so that, in many instances, they are able to resume adequate functioning.

Nursing Bottles

Breast feeding of the new-born infant is not always possible or feasible, so nursing bottles and nipples must be used. A new development in this respect is the sterile, disposable nursing bottle which collapses as the milk is withdrawn. It is discarded after one feeding. Made of plastic, it is sterilized and sealed against exposure until used. A new, non-collapsible nipple is used with this bottle and allows the baby to nurse more naturally.

Respirator

A completely new kind of respirator recently was tried in the alleviation of bulbar poliomyelitis, the most dangerous form. In this type of poliomyelitis the iron lung is contraindicated because its rhythmic pumping may interfere with the patient's irregular breathing. For this reason at the Children's Hospital in Boston it was decided to try a new respirator composed of an electronic apparatus which produces normal breathing by direct stimulation of the phrenic nerve leading from the brain to the diaphragm. This Electrophrenic Respirator, developed by Drs. S. S. Sarnoff, J. L. Whittenberger, and Esther Hardenburg at Harvard University's School of Public Health, consists of an electrode and a compact control box which serves to regulate the electric pulses which cause the rhythmic contraction of the diaphragm. This piece of apparatus will not replace the iron lung but will have its own specific uses in various conditions other than poliomyelitis, such as the maintenance of respiration during brain surgery, in emergency cases and in aiding newborn babies to take their first breath.

Sub-Q-Pak

Repeated sterilization of the equipment for hypodermoclysis is a problem in the hospitals, and in some cases complete sterilization is not always accomplished. For this reason there has been developed a completely disposable hypodermoclysis unit for the subcutaneous administration of fluids. The unit consists of a dispensing cap, air filter, Murphy drip, plastic tubing with a "y" assembly, two pinch clamps and needle adapters with protective covering. It is packed sterile, preassembled and ready for use. All equipment, except needles, is discarded after use. Under the name of Sub-Q-Pak these units are available from Abbott Laboratories.

PARASYMPATHOMIMETIC

Urecholine

Urethane of β-methylcholine chloride or bethanechol chloride is a new and potent parasympathomimetic drug used for the prevention or alleviation of distressing postoperative gas pains and abdominal distention due to loss of smooth muscle tone. Clinical tests have shown that bethanechol chloride is extremely helpful in many cases

because it improves muscular tone and stimulates normal rhythmic peristalsis. In a limited investigation in the treatment of megacolon, certain patients have responded favorably, a few obtaining complete symptomatic relief. The drug has proved valuable also in the relief of symptoms which often follow vagotomy, one of the operations sometimes performed for peptic ulcer, and frequently it is useful to prevent or relieve postoperative urinary retention. It is given orally or subcutaneously. Under the name of Urecholine Chloride, this drug is available from Merck and Co., Inc.

PRURITUS

My-B-Den

A new approach to effective treatment of pruritus was recently announced. In the majority of cases studied thus far, adenosine-5-monophosphate has produced complete subsidence or marked amelioration of symptoms. Beneficial results have been reported in generalized pruritus, pruritus ani, pruritus vulvae, pruritus scroti and in cases of Hodgkin's disease, dermatitis herpetiformis, diabetes mellitus, obstructive jaundice and hair dye sensitivity. It is thought to correct the altered phosphorylation mechanism responsible for pruritus and certain forms of skin disease. This unique biochemical is intimately related to basic life processes and is a vital metabolic link in muscular contraction and enzymic reactions. Clinical and pharmacological studies indicate an important role for this compound in the treatment of vascular disturbances, cardiovascular disorders and degenerative diseases. Known as My-B-Den, it is supplied by Ernst Bischoff Company, Inc.

Protegel

A soothing paste composed of alumina gel with kaolin is recommended for application to the skin about intestinal fistulas and for moist pruritus ani. It dries to form a protective coating that resists the corrosive action of oozing intestinal secretions and relieves itching and burning. It is marketed as Protegel by Wyeth, Inc.

PSORIASIS

Undecylenic Acid

That the oral administration of undecylenic acid is of value in the treatment of certain skin diseases and other disease entities is a

new concept. Heretofore, undecylenic acid has been used only by topical application. The local use in the treatment of ringworm infections of numerous types of the acid, alone and in combination with its metallic salts, grew from demonstration that they possess fungicidal activity. During an investigation of topical medication for the treatment of tinea capitis (*Microsporon audouini*), the fungistatic properties of undecylenic acid were found inoperative against the causative organism. This was thought to be due to inaccessibility of the organism encased within the hair follicle. Simultaneously it was reported that, at the onset of puberty, sebaceous secretions of the scalp contain higher concentrations of certain saturated fatty acids and that these acids have fungistatic and fungicidal action against *M. audouini*. Since tinea capitis is regressive at puberty, it was reasoned that the oral administration of one of the saturated or unsaturated fattty acids might be therapeutically effective in its treatment. Because of its known fungicidal activity and because it is an unsaturated fatty acid in the same carbon chain range as fatty acids in sebaceous secretions of the scalp, undecylenic acid was chosen. Toxicity tests revealed that it was relatively nontoxic. The most positive effect of treatment with undecylenic acid, profuse desquamation of the scalp, was a consequence which would be desirable if it could be effected in other skin diseases. Thus an investigation of its value in psoriasis began, and the results were promising. It has also shown some value in neurodermatitis, arthritis and bursitis. Its use, while empirical, is based on well demonstrated improvement in disturbances for which no specific therapy is available. Further clinical and scientific research is indicated to determine the usefulness of the drug, its safety, and the optimum dosage.

The ingestion of undecylenic acid produced some side actions, such as belching, nausea, vomiting, burning sensation in the epigastrium, and bad taste in the mouth. These were relieved or prevented by using carbonated water, soft drinks, or sodium bicarbonate in water along with capsules containing the acid. Other untoward reactions of which the patients complained were frontal or occipital headache, a sense of fullness referred to the frontal area of the head and above the eyes, diarrhea, folliculitis, localized minute abscesses upon the posterior aspect of the neck, conjunctivitis, axillary adenitis, and frequent micturition. These usually disappeared in a short time,

even though the medication was continued. When vomiting occurred, medication was stopped. With its resumption, vomiting did not occur. It is possible that some of these side effects were coincidental ones. Routine observation of blood pressure, respiration, heart action, pulse rate, temperature, and urinalysis failed to indicate any abnormalities.

Undecylenic acid is the common name for 10-undecenoic or 10-hendecenoic acid, $CH_2{=}CH(CH_2)_8COOH$. It is a straight chain, 11-carbon atom, terminally unsaturated fatty acid. Undecylenic acid is an extremely weak acid and is insoluble in water. It is a liquid at room temperature (m. p. 24.5° C.). It has a characteristic odor and a persistent bitter or acrid taste. Consequently, it must be purified and encapsulated for oral administration. Undecylenic acid is related to oleic acid, the fatty acid contained in lard and olive oil. However, it differs from naturally occurring fatty acids (oleic, stearic, palmitic, etc.) in that it has a lower and an odd number of carbon atoms. It differs, too, in its point of unsaturation since the compound is unsaturated at the end of the carbon atom chain.

The toxicity of undecylenic acid is low. The largest practical quantities of the compound which could be force-fed to mice failed to kill the animals. The oral LD_{50} is approximately 3 Gm./Kg. and 0.75 Gm./Kg. for rats and guinea pigs, respectively. Rabbits showed no ill effects with 0.9 mg./Kg. by mouth. In chronic toxicity studies, laboratory animals showed no pathologic changes. The absence of severe side actions following large daily dosages for periods of six months or longer demonstrated the relative safety of the acid in man.

It is not understood how undecylenic acid produces desquamation or ultimate clinical benefit. The precise nature of any metabolic changes brought about by the compound remains to be determined. The fact that this fatty acid is a liquid is a factor which probably influences the rate of its digestion and absorption.

Specially purified undecylenic acid certified for oral use is not to be confused with undecylenic acid preparations which have been used locally for a long while in the treatment of skin infections. Undecylenic acid, as available on the open market, varies in chemical composition. The specially fractionated product possesses physical and chemical properties known to produce the clinical effects which

have been obtained. It is not known whether less pure undecylenic acid available for external use has a similar effect. This special product is available under the name of Declid from Decyl Pharmacal Company, Princeton, N. J., and as Sevinon from Schering Corporation, Bloomfield, N. J.

Radioactive Compounds

There have been many advances in the field of radioactivity in the past year. It has been reported that radioactive mosquitoes are being used by the Rockefeller Foundation to fight yellow fever. Insects in the larval stage are exposed to weak solutions of radioactive phosphorus, and as a result the adults which develop are radioactive for the duration of life. These, when they are released and recaptured, can be identified. By this means it is possible to determine the rate and direction of the spread of a mosquito colony and the average length of life. It is, of course, a laborious task since 175 man hours are required for the recapture of fifteen radioactive insects out of a colony of 5,000 which has been treated with the phosphorus bath.

Studies have been made to develop methods of increasing human resistance to radiation. In animals it has been found that horse serum, administered 10 days before the radiation treatment, reduces mortality in 40 days to zero, compared with 21 per cent and 28 per cent losses among male and female controls. If the serum is given immediately after radiation, deaths more than double in comparison with the controls. Administration of certain steroids or foreign proteins, such as the male and female hormones and adrenal gland cortical hormone, before or after radiation also enhance or diminish its effects. It is believed and hoped that these discoveries may influence, in some manner, the survival from total body radiation and the effectiveness of radiation treatment of cancer.

The effects on radiation in animals of folic acid and pyridoxine also have been studied. Folic acid given after radiation had no obvious effect on the blood picture as there was with the controls, but there was seemingly a significant reduction of the number of deaths during one of the phases of radiation sickness from 26 per cent to 2 per cent or less. The animals given folic acid survived longer too. Survival times were greatly prolonged in animals given pyridoxine before radiation but not after irradiation. The propor-

tion of animals surviving the radiation treatment after 100 days was increased from 19 per cent in the control group to 58 per cent in the pyridoxine-treated group and 62 per cent in the folic-acid-treated group.

Rutin also has some effect in counteracting the effects of radiation. Asparagus recently was reported to be one of the richest sources of this drug. Rutin acts by strengthening the walls of the capillaries and thus prevents the small, innumerable internal hemorrhages caused by radiation.

Use of irradiation by ultra-violet light to kill or destroy the reproductive ability of certain micro-organisms has been in vogue for several years. A limited number of these organisms will recover in a few days. Recently it was reported that ordinary light immediately after ultraviolet radiation will increase this recovery rate as much as 400,000-fold. If the organisms are kept in the dark this does not occur. The ultraviolet rays act by disrupting the vital process of single-celled organisms, and something in ordinary light restores the process. It is hoped that this may, some day, aid in discovery of the factors involved in recovery from x-irradiation or irradiation from radio-active materials.

Recently it was reported that polycythemia vera, a rare and fatal blood disease, has been controlled by sodium radiophosphate. When this compound is administered to such patients, it collects in the bone, bone marow and some rapidly growing tissue and inhibits the production of red cells. This is a therapy which, it is hoped, will mean as much to the patients with polycythemia vera as insulin does to diabetics.

Within the past four years Abbott Laboratories has estabished a special research department to study the use of radioactive isotopes in medical diagnoses and therapy. This program also is directed toward:

1. The use of isotopes as a tool to secure even more complete information regarding the nature and mode of action of therapeutic substances. For instance, Pentothal has been prepared containing radioactive S-35, and studies now nearing completion shed new light on its mode of action and elimination. Similar studies are underway or already published involving Nembutal, Chiniofon, and other useful drugs.

2. The preparation of sterile, pyrogen-free, stable and accurately standardized solutions of certain widely used isotopes such as P-32 and I-131. These are packed in suitable lead shields which permit safe shipment and use by medical units.

3. Chemical synthesis whereby specific isotopes are incorporated into compounds or special forms which permit their use for new purposes. For instance, di-iodo-fluorescein containing I-131 is being regularly prepared; given intravenously in proper dosage it localizes in certain types of brain tumors and other lesions. A sensitive Geiger tube placed at various positions outside the skull picks up the gamma radiations from the iodine in the tumor which then may be located within a considerable degree of accuracy, (Nucleonics 1948, p. 63). Hahn and his associates pioneered the use of radioactive Colloidal Gold-198 which is also being prepared regularly by Abbott Laboratories. This solution containing as much as 10-20 millicuries of activity per cc., is injected directly into the tumor mass which is thus subjected to intense local irradiation. The short "half life" of the gold makes unnecessary its mechanical removal.

4. A number of special compounds such as gold sodium thiosulfate, methionine, thiourea, and tetraiodo phenolphthlein have been "tagged" for specialized research purposes; this part of the work will be expanded as rapidly as possible.

It is to be emphasized that the clinical use of such radioactive materials is still experimental. Treatment of polycythemia vera with P-32 is as successful and somewhat more convenient than general irradiation. Its use in leukemia is on a less firm basis. Under properly controlled conditions Na I-131 may be used to reduce or destroy thyroid activity. Thyroid tumors which take up iodine have been successfully treated in the same way. In much smaller doses it may be used to accurately measure thyroid activity.

The original isotopes are secured from the U. S. Atomic Energy Commission piles at Oak Ridge or Chicago, in units which may have several hundred millicuries of activity, and are processed in the laboratories. Shipments of the processed materials can be made only to individuals or groups who have received specific allocations from the U. S. Atomic Energy Commission, Isotopes Division. Countries in the Pan American Union which have completed

arrangements for the receipt of isotopes are Argentina, Brazil, Chile, Colombia, Cuba, Guatemala, Mexico and Peru. Individuals or groups should submit their requests to the United States Atomic Energy Commission, Isotopes Division, Oak Ridge, Tennessee, by or through the representative designated by their government for that purpose. This request must establish that not only will proper use be made of the material but that adequate facilities for its safe handling are available.

If the materials are to be secured from or processed by Abbott Laboratories the application should so state, and a carbon copy sent directly to Dr. D. L. Tabern, Abbott Laboratories, North Chicago, Illinois.

Eurax Cream

Numerous effective products have been marketed for the eradication of scabies. Recently a new cream containing 10 per cent of N-ethyl-o-crotontoluide and having a highly efficient miticidal action, as well as a bacteriostatic effect on other organisms such as staphylococci and streptococci, has been announced. It is odorless, non-greasy, non-soiling, non-staining, non-toxic and non-irritating. It is available as Eurax Cream from Geigy Co., Inc., Pharmaceutical Division.

SCABICIDES

Kwell

Another new scabicide is 1,2,3,4,5,6-hexachloro-cyclohexane which has been used effectively. It is incorporated in a vanishing cream base to the extent of 1 per cent. Without preliminary bathing, a thin film of the cream is rubbed into the entire cutaneous surface. About 15 to 25 Gm. are required for one adult treatment. The patient is not to bathe for 24 hours. After a thorough bath all underclothing, night clothes and bed linen are to be changed and thoroughly laundered. The patient is examined, after one week to allow ample time for any ova to hatch. This remedy is effective in cases in which other remedies fail. In the clinical trials no cases of irritation or sensitivity have been recorded, and there were no contraindications even in the presence of severe dermatitis from scratching. This drug also has proven to be effective in the control of chiggers, ticks, fleas, cockroaches, bedbugs, and pediculi capitis, corporis and pubic. The toxicity of the drug is quite low when

applied to the skin or even when administered orally, according to tests on experimental animals. The drug is marketed by Commercial Solvents Corporation in Kwell Ointment.

VASOCONSTRICTORS, VASODILATORS

Benzedrex

For many years there has been available an inhaler containing volatile racemic amphetamine or chemically *dl*-1-phenyl-2-aminopropane. It was indicated for use as a vasoconstrictor for shrinking the nasal mucosa in head colds, sinusitis, aero-otitis and allergic rhinitis. Because this drug also possessed a stimulating effect upon the central nervous system it was misused by school students, juvenile delinquents and others for so-called "jags" and resulted in considerable criticism of the pharmacist for selling such inhalers without a prescription. In order to remedy the situation the manufacturer instituted extensive research to find a substitute which would have the vasoconstricting effect without the stimulating effect. Recently a new inhaler containing volatile 1-cyclohexyl-2-methylaminopropane 250 mg. and aromatics was made available, and the earlier Benzedrine inhaler was withdrawn from the market.

The new compound has the same indications and produces the same rapid, complete and prolonged shrinkage of the nasal mucosa. However, it produces almost no central nervous stimulation and, therefore, does not cause insomnia, restlessness or nervousness even after repeated usage. Known as the Benzedrex Inhaler, this product is marketed by Smith, Kline and French Laboratories.

Roniacol Tartrate

A new product of this group, Roniacol tartrate, recently introduced is, chemically the alcohol corresponding to nicotinic acid but is distinguished from nicotinic acid by a far lower incidence of side effects. If flushing of the face and neck occurs at all, it is usually mild and does not inconvenience the patient. A significant advantage is that its action is much more prolonged than that of nicotinic acid. Moreover, patients are not likely to develop a tolerance, so it can be used over prolonged periods without requiring frequent increases in dosage. This new drug is available as Roniacol Tartrate from Hoffmann-La Roche Inc.

Serotonin

A crystalline substance has been isolated from beef serum and shown to have some vasoconstrictor activity. In animal experiments it has been shown to cause an effect similar to that caused by more than twice an equal weight of epinephrine hydrochloride. Known as Serotonin this substance is being investigated by the Research Division of the Cleveland Clinic Foundation.

VEHICLES

Bacteriostatic Base

A patent was recently issued covering a new bacteriostatic base for medicinal, cosmetic and toilet preparations. This base is a fluid and is not only of value as a vehicle but also as a stabilizer for labile medicaments and antibiotics. It combines the properties of a carrier and of a wetting and penetrating agent; in addition, it has bacteriostatic action which is not inhibited in *in vitro* tests by the presence of 10 per cent defibrinated blood. It also is said to be compatible with soap solutions and creams forming therewith improved shaving creams, shampoo compositions, etc. The patent also covers a new fused bentonite sulfur composition, made by compounding fused bentonite sulfur with the fluid base. The following formula is an example of a stable fused bentonite sulfur cream:

Fused bentonite sulfur	20.4%
Urea	8.2%
Sodium taurocholate	2.0%
1% quince seed extract	40.9%
Glycerin	6.1%
Ethyl alcohol	16.7%
Distilled water	5.7%
Synthetic oil of rose Neil (optional)	Trace
Coloring agent (optional)	Trace

Also included in the patent is:

Fused bentonite sulfur cream	40 parts
Concentrated fluid base	16 parts
Liquid soap shampoo (35 per cent mild synthetic castile)	44 parts

The preparations containing this fluid base are believed to be of therapeutic value in the treatment of ringworm infections, both on human beings and on animals, the treatment of barber's itch, scabies,

acne, various fungus infections of unknown etiology, and in the treatment of athlete's foot, dermatitis, insect bites and plant poisoning.

Hydroabietyl Alcohols

A substance comparatively new to pharmaceutical practice, hydroabietyl alcohol, may serve to supply improved properties to preparations and products not only in the dispensing laboratory but possibly in the cosmetic field as well. Hydroabietyl alcohol, as supplied to the trade, is a crystal clear product containing approximately 85 per cent of resin alcohols and 15 per cent of non-alcoholic material. The resin mixture has an approximate composition of 15 per cent dehydroabietyl alcohol, 40 per cent dihydroabietyl alcohol and 45 per cent tetrahydroabietyl alcohol. Hydroabietyl alcohol is a colorless, tacky, viscous liquid at ordinary temperatures. The functional alcohol group is typical of any primary monohydric alcohol together with what might be expected from the residual unsaturation of the conjugated ring structure. It may be esterified, etherized, halogenated, hydrogenated, dehydrogenated and polymerized. Hydroabietyl alcohol is insoluble in water, ethylene glycol and propylene glycol and glycerin. Although hydroabietyl alcohol is a very tacky product, its tackiness is unnoticeable when warmed to the boiling point of water. Its water-clear color is best retained in the atmosphere of an inert gas as nitrogen or carbon dioxide. However, color change, at ordinary temperatures, is so slow that no discoloration has appeared at the end of a year's exposure to the atmosphere. The resin alcohols are soluble in a wide range of organic chemical solvents familiar to the pharmacist as methyl, ethyl, isopropyl and butyl alcohols, turpentine, acetone, ether, chloroform, carbon tetrachloride, linseed and the familiar vegetable oleins. Hydroabietyl alcohol is compatible with ethyl cellulose and cellulose nitrate but not with cellulose acetate. It is miscible with shellac and carnauba wax in all proportions. Hydroabietyl alcohol may serve as a useful agent in a number of pharmaceutical preparations where its unusual properties serve to modify and improve the composition, character or efficiency of the standardized or "official" formulas. Some of these products include the various collodions and other formulas, lotions and emulsions commonly employed in dermatologic practice where viscosity and tackiness may be desired. Pos-

sibly the use of this product may be helpful in improving the adhesiveness of finger nail polish and enamels. If such proves to be the case, the life of such enamels would be considerably prolonged. Further chemical reactions of these substances to produce derivatives which may be of value in numerous products are being studied. The hydroabietyl alcohols are marketed by the Hercules Powder Co.

Plastic Film Base

The requirements for plastic films vary with the specific requirements of the therapy for which the film is to be used. In most cases the film should be transparent so that healing may be observed; it should be elastic but also tough so that it will be long-lasting; it should be set quickly when applied so that it will remain in the desired position; it should form a non-porous film over the area to prevent contamination and infection; its pH should be suitable for application to the skin; it should be unaffected by oils, greases and fats and should be so that the film could be made water-resistant if desired; and the medication should be in a uniform suspension or solution and should be released slowly and steadily.

The Canadian workers Huston, Riedel, Murray and Groves recently reported on preliminary experiments on plastic film bases. They reached certain conclusions relative to the effect on the properties of bases by certain substances. Polyvinyl alcohol was found to produce the most satisfactory film relative to elasticity and transparency. Films produced with methyl cellulose are lighter, more porous and less elastic than polyvinyl alcohol films. Borax solutions cause polyvinyl alcohol films to set almost immediately while methyl cellulose along with polyvinyl alcohol increases the viscosity. Plasticizers were found to increase the pliability of the films but also to increase the drying time. The films dry in 10 to 15 minutes and were suitable vehicles for 1 per cent sulfathiazole. Two of the more satisfactory formulas were:

Propylene glycol	5.9
Castor oil	2.0
Polyvinyl alcohol (5 per cent) q. s. to make	100.0

Triethanolamine	2.0
Hexaethylene glycol	4.0
Borax solution	10.0
Polyvinyl alcohol (4 per cent) q. s. to make	100.0

Polawax

A new form of the self-emulsifying cetyl-stearyl, alcohol combinations is now available. It is non-ionizing and non-hydrolyzing. It is a waxy solid faintly cream in color and is a specially modified stearyl alcohol of enhanced polar properties—its oil-in-water emulsion producing properties do not arise from the presence of auxiliary anionic emulsifiers of the soap or sulfonated sulfated fatty alcohol type. This new emulsifying wax is the only one of three which can be employed to make an ointment containing the strong electrolyte sodium sulfacetimide.

Sodium sulfacetimide	20 gm.
Emulsifying wax	12 gm.
Liquid petrolatum	10 cc.
Distilled water	66 cc.

The sodium sulfacetimide is dissolved in the distilled water heated to approximately 70°C. The solution is stirred into the previously melted emulsifying wax and liquid petrolatum. The emulsion formed is stable for 4 months. Known as Polawax, this is marketed by Croda, Ltd.

Postonal

A synthetic, fat-free, water-soluble vehicle which resists summer and tropical climates has been developed in Germany for use in suppositories. It is clean and quick processing and has practically unlimited solubility. The incorporated drugs are completely resorbed in the intestines. This vehicle is available as Postonal from Farbwerke Hoechst, Frankfurt, Germany.

VITAMINS

Extensive studies of the chemical processes involved in vision by Harvard University workers have revealed that niacin, a member of the vitamin B complex and well-known for its role in the prevention of pellagra, is also of importance in the mechanism of vision. Rhodopsin, the red substance in the retina of the eye which bleaches when exposed to light and starts the chemical processes by which humans see, first forms a yellow substance known as retinene. This is then converted to colorless vitamin A necessary for vision at night. Vitamin A, in turn, is joined with a protein to form more

rhodopsin thus completing a cycle, and vision continues indefinitely. Vitamin A also is present in high concentration in the retina, and a deficiency of it causes night blindness. Recently Dr. G. Wald of Harvard found that niacin is instrumental in the conversion of retinene to vitamin A by transferring 2 hydrogen atoms to the retinene. This reaction is accomplished by means of an enzyme and a co-enzyme, and niacin is the key component of the latter. Thus this discovery not only adds to the knowledge of how the eye functions but also will be of value in the therapy of various eye conditions and in particular, night-blindness.

Biocytin

Although it may never achieve great prominence, the discovery of a new vitamin factor, biocytin, should be acknowledged in a review of this type. It was isolated from yeast extract in which it is present in the minute quantity of one part per million of dry extract. In order to obtain a fraction of a gram it was necessary to process more than 8 tons of yeast extract. Biocytin was isolated by the research staffs of Sharp and Dohme and Merck and Co. Clinical studies are now under way to determine possible medical uses.

Hyflavin

Since the discovery of riboflavin one of the greatest difficulties in its administration has been the problem of solubility. Various solutions have been developed with some success. Wthin the past year a new highly soluble derivative has been made available for intravenous or intramuscular injection. This new form permits the preparation of concentrated solutions without resorting to unduly large amounts of niacinamide or other foreign solubilizing agents. It also overcomes the objectionable features and inconvenience of the lyophilized riboflavin injections. Available under the name Hyflavin Injection Solution this product is marketed by Endo Products, Inc.

MISCELLANY

Ether

A new, non-surgical treatment for obstruction of arterial circulation in the legs has been reported by Dr. R. A. Katz of the Truro Infirmary and Dr. O. C. Williams of the United States Public Health

Service. The treatment consists of the injection into the vein, by the drip method, of a 2½ per cent solution of ether in distilled water containing 5 per cent glucose, or dextrose. It is administered at the rate of 40 to 60 drops a minute to a total of 1,000 cc. a day. The course of treatment includes 12 daily injections, and after an interval of rest the course may be repeated. This therapy also has given encouraging results in arteriosclerosis, thrombo-angiitis obliterans or Buerger's disease, diabetes, varicose ulcers, perivascular disease, neurodermatitis, neuritis, Raynaud's disease, periarteritis, traumatic gangrene and angiospasm.

Gray Hair Preventive

Dr. H. I. Jones has recently reported that a substance derived from a mold bran, used as a special feed for prize cattle, has been effective in restoring gray hair on cattle to its natural color. This is now being tested at Iowa State College as a possible ingredient of a breakfast food and for its possible use to prevent gray hair in humans.

Calcium Gluconate

Calcium gluconate is not a new drug by any means, but a new use for it has been discovered. Victims of the deadly bite of the Black Widow spider no longer need fear toxic effects if they can reach a physician. It has been found that injections of calcium gluconate relieve the symptoms and effect a cure. However, it is necessary that treatment be given immediately.

Lucaine

Chemically related to procaine, intracaine and similar ester compounds β-2-piperidyl-ethyl-orthoamino-benzoate-hydrochloride is a new local anesthetic Unlike procaine and pontocaine, it is an ester of ortho-amino-benzoic acid The compound is a white powder which dissolves in water with difficulty However, solutions of 1 per cent or less may be made in water or spinal fluid These are sufficiently concentrated for clinical use. Its solubility precludes the use of more concentrated solutions. When given intrathecally in a 0.5 per cent solution this drug produces sensory anesthesia with mild paresis or sensory anesthesia with no motor involvement at all. Known as Lucaine it is being investigated by Maltbie Laboratories Inc.

Mineral Oil

Recent investigation of pneumonia in elderly persons has traced the cause in some cases to repeated doses of mineral oil. Further studies are now being made. Dr. L. Schneider reported that the pneumonia may be present for a long time before it causes changes that are recognizable on an X-ray film, and the examining physician may mistake the disease for cancer of the lung or bronchus and subject the patient to a needless operation. Pneumonia was revealed by chest examinations in 5 elderly patients who were apparently in good health but reported that they had taken mineral oil regularly for laxative purposes.

Monitan

The first palatable liquid solution of sorbitan monooleate polyoxyethylene derivative (S. M. P. D.), a wetting agent which quickly and easily emulsifies and reduces the particle size of fats and fat soluble materials, is now available. It is indicated for use in abnormal physiological conditions characterized by impaired absorption of fats or fat soluble substances from the small intestines. The most striking sign of inefficient fat absorption is steatorrhea, a symptom in which excess amounts of fat are found in the stools. The solution is indicated in malnutrition due to faulty fat absorption; intestinal hyper- or hypoactivity; reduced absorbing surface in small bowel; dimunition of digestive enzymes; regional enteritis; pancreatic fibrosis; sprue; celiac disease; and impaired biliary cycle. It also is beneficial to patients following subtotal gastrectomy and will maintain postcholecystectomy patients on a complete diet. Fecal fat in excess of the normally accepted figure of 4 per cent is a definite indication. Marketed as Monitan it is supplied by Ives-Cameron Company, Inc.

Olothorb

Polyoxyethylene sorbitan monooleate also is now available in capsule form. Each capsule contains 0.5 Gm. of the active ingredient, and the minimal dosage daily dosage is 6.0 Gm. (2.0 Gm. or 4 capsules three times a day with meals). In addition, an adequate diet should be provided, including a minimum of from 125 to 150 Gm. of fat. This product acts in the same manner and is indicated in the same conditions as the previously described product. Under

the name of Olothorb, the caspule product is marketed by Sharp and Dohme, Inc.

A. T. P.

Adenoisine-tri-phosphate is responsible for providing the energy for muscular contractions in the human body. Normally it is produced by the body and stored in the muscles. Within the last year synthesis of this material has been accomplished, and some degree of success has been achieved in treating various heart conditions according to Dr. A. Todd of Cambridge University.

Cabbage Juice

In various tests with the general run of peptic ulcers several authorities have revealed that the average healing time for duodenal ulcers was 37 days and for stomach ulcers, 42 days. Dr. Garnett Cheney of the Stanford University Medical School has reported that this healing time has been reduced considerably by the administration of raw cabbage juice. When it was given to 13 patients, only one case required 23 days of therapy. In this case, at the end of 8 days the lesion had disappeared, but a bump-like deformity remained. In the 6 duodenal ulcer cases the average healing time was 10.4 days and for the 6 stomach ulcer cases was 7.3 days.

Desoxyribonucleic Acid

Originally called thymus nucleic acid because the "sweetbreads" or thymus glands of calves were the usual source, desoxyribonucleic acid or DNA is now known to occur in the genes of all cell nuclei and is the cell component basic to inheritance along with the related ribonucleic acid (RNA, or yeast nuclei acid). Both are available from Schwarz Laboratories, Inc.

Cafergone

The latest advance in the therapy of migraine headache is the development of a preparation containing 1 mg. ergotamine tartrate and 100 mg. caffeine. Experimentally the product was known as E. C. 110. This drug is the first oral preparation to give reliable relief of the migraine headache attack. A number of clinical studies have demonstrated a high percentage effectiveness in this and other vascular type headaches (tension and histaminic headaches). Best

results are obtained by giving an adequate amount, preferably in a single dose, as early as possible in the attack (at the very first sign of pain). Administration between attacks as prophylactic treatment is not recommended. Doses exceeding 4 tablets may produce transient tachycardia and restlessness in certain susceptible persons due to the caffeine component. The drug may be given to interrupt the progress of an attack once started, thereby markedly shortening it and reducing it in severity. It should not be administered in the presence of peripheral vascular disease, angina pectoris, impaired renal or hepatic function, or during pregnancy. This new preparation is available as Cafergone from Sandoz Pharmaceuticals.

Methyl Cellulose

The synthetic hydrophilic colloid methyl cellulose has a high degree of chemical uniformity which is not found in natural gums. This is one of the advantages of the use of methyl cellulose as a bulk laxative. It has been reported that the way in which the colloid takes up water makes it almost impossible to form an impaction. Methyl cellulose forms a colloidal solution in any amount of water, the viscosity varying from a soft smooth gel to a thin demulcent liquid. Following use, the stools passed are normal, soft and bulky and are passed without accompanying griping, cramping or tenesmus. Methyl cellulose is available under the name Cellothyl from Chilcott Laboratories.

Eskalose Wafers

Another laxative contains sodium carboxy-methyl cellulose. It is available as Eskalose Wafers from Smith, Kline and French Laboratories.

G-Salt

The sodium salt of 2-naphthol-6,8-disulfonic acid has been found to provide protection from solar urticaria when incorporated in a concentration of 30 per cent in Ruggles' Cream. It is marketed by National Aniline Division, Allied Chemical and Dye Corp. as G-Salt.

Niaarin

A new glycoside obtained from the latex of the South American tree *Ogcodeia ternstroemiiflora* has been employed successfully

in the treatment of congestive heart failure, according to a report by K. Mezey and his associates. Used by Colombian natives as an arrow poison this extract has chemical and pharmacological properties similar to those of the cardiac glycosides. It has no curariform activity and is like strophanthin in its rapidity and brevity of action. Seven patients were treated with 0.5 to 0.75 mg. daily for two days and then with 0.25 mg. daily for two or three days more. Substantial drops in heart and respiratory rates, venous pressure and circulation time were noted within 24 hours after beginning therapy. No side effects were observed. Intravenous administration is necessary because the drug is poorly absorbed from the gastrointestinal tract. This new compound has been given the name Niaarin.

Antabuse

Reports from Copenhagen revealed that a chemical, diethylthiurandisulfide or bis(diethylthiocarbanyldisulfide), was believed to be of value in treating alcoholism. Clinical trials revealed that it did have value in this therapy, but later it was shown there could also be undesirable effects. It was found that 0.5 to 1.5 Gm. of this substance cause characteristic unpleasant symptoms when people subsequently drink even small amounts of alcohol. This drug should not be given to patients with disorders of the cardiovascular system, liver, kidneys, blood-forming organs, nor to diabetics. This warning is given because of the nature of the reaction which occurs following the ingestion of alcohol during treatment with Antabuse. Among the effects produced are acceleration of the pulse, elevation of the skin temperature, edema under the eyes, nausea and vomiting. Biochemically the major change seems to be an elevation of the blood level of acetaldehyde.

In the treatment of alcoholics a large initial dose of 2 Gm. of the compound should be given. Alcohol should then be given deliberately so that the patient may experience the severe reaction which will be his lot any time thereafter should he partake of alcohol. This should be performed under hospital care. Subsequent dosage is 1.5 Gm. on the 2nd day, 1.0 Gm. on the 3rd, and 0.5 to 0.7 Gm. thereafter. The maximum effect of the drug is obtained 6 to 12 hours after administration. Further investigation of this chemical known as Antabuse is being made under the direction of Ayerst, McKenna and Harrison in the United States and Canada.

Polyestol Bandage

Recently there was introduced a highly elastic, transparent plastic material (polyestol), which gives off, at a constant rate, about one-third its weight of methyl salicylate. This bandage is indicated in such common conditions as rheumatoid ailments and acute rheumatic fever, fibrositis, lumbago, gout, myalgia, neuralgia, muscle stiffness, sprains, strains, etc. It can be used for 60 hours but not more than 10 hours at a time. Known as Polyestol Bandage it is supplied by Duncan C. McLintock Co., Inc.

BOOK REVIEWS

The British Pharmaceutical Codex 1949. Published by Direction of the Council of the Pharmaceutical Society of Great Britain; 1562 pages; The Pharmaceutical Press, 17 Bloomsbury Sq. W. C. 1, London. £3.3.0.

This is the first complete revision of the Codex since 1934, although a total of seven supplements were issued to the Codex of 1934 between the years 1940 and 1945.

The new Codex should prove a very welcome and useful volume to British pharmacists and medical practitioners by whom the book is extensively used and highly esteemed. American pharmacists do not have a book which is comparable, unless it be the United States Dispensatory.

For the benefit of those not familiar with the scope of the British Pharmaceutical Codex, it may be pointed out that the Codex describes those drugs recognized in the British Pharmacopoeia as well as many others which are used but not given official recognition. The Codex, therefore, includes both official and non-official drugs.

There is hardly any comparison in the scope of the Codex of 1934 and this of 1949 since there has been an almost unbelievable amount of progress in the field of medicinals during this fifteen year period. Of course the supplements do much to amend the 1934 Codex, but it is much more convenient to have all of this material incorporated and arranged in a single volume.

The Codex is divided into seven parts, which are as follows:

I General Monographs
II Antisera, Vaccines and Related Substances
III Preparations of Human Blood
IV Surgical Ligatures and Sutures
V Surgical Dressings
VI Formulary
VII Appendices

Each of these sections has been completely revised in accordance with modern practice.

The section devoted to the formulary has been considerably changed, but it is still somewhat striking to the American pharmacist

that our British colleagues still place considerable emphasis on galenicals.

In looking through the book, it is evident that a very careful revision of the Codex has been accomplished, but this reviewer would expect nothing less since the works originating under the auspices of the Pharmaceutical Society of Great Britain have always been of the highest quality. The Codex should prove a most useful reference work in all Pharmaceutical libraries throughout the world.

L. F. TICE

Natural Products Related to Phenanthrene, 3rd Edition. By Louis F. Feiser and Mary Feiser, xii + 704 pages, 1949, New York. Rheinhold Publishing Corp. $10.00.

Cortisone, one of the outstanding drugs of 1949, which has drawn the interest of many workers in medical, pharmaceutical and allied sciences is an example of this important group of substances. Also related to phenanthrene are such important compounds as the cardiac glycosides, certain alkaloids, many hormones, vitamin D and the saponins.

This monograph was first published in 1936 by the American Chemical Society as "The Chemistry of Natural Products Related to Phenanthrene". In revision for the present book, several original sections were omitted to make room for voluminous new material, however this edition is still almost twice as large as its predecessors.

Although most of the subject matter deals with chemistry, much pharmacological information is included, and the authors emphasize chemical structure and physiological activity relationships where they exist. The style, typical of the authors, is clear and terse. Ten chapters include; Quinones-Morphine and Related Alkaloids, Resin Acids, Sterols and Bile Acids, Sex Hormones, Adrenal Corticle Hormones, Steroid Metabolism, Cardiac Active Principles, Steroid Saponins, Steroid and Terpenoid Alkaloids, and Stereochemistry of Steroids.

This volume should be well received by readers in many fields who are concerned with natural phenanthroid products.

N. HALL

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Philadelphia, Pa.

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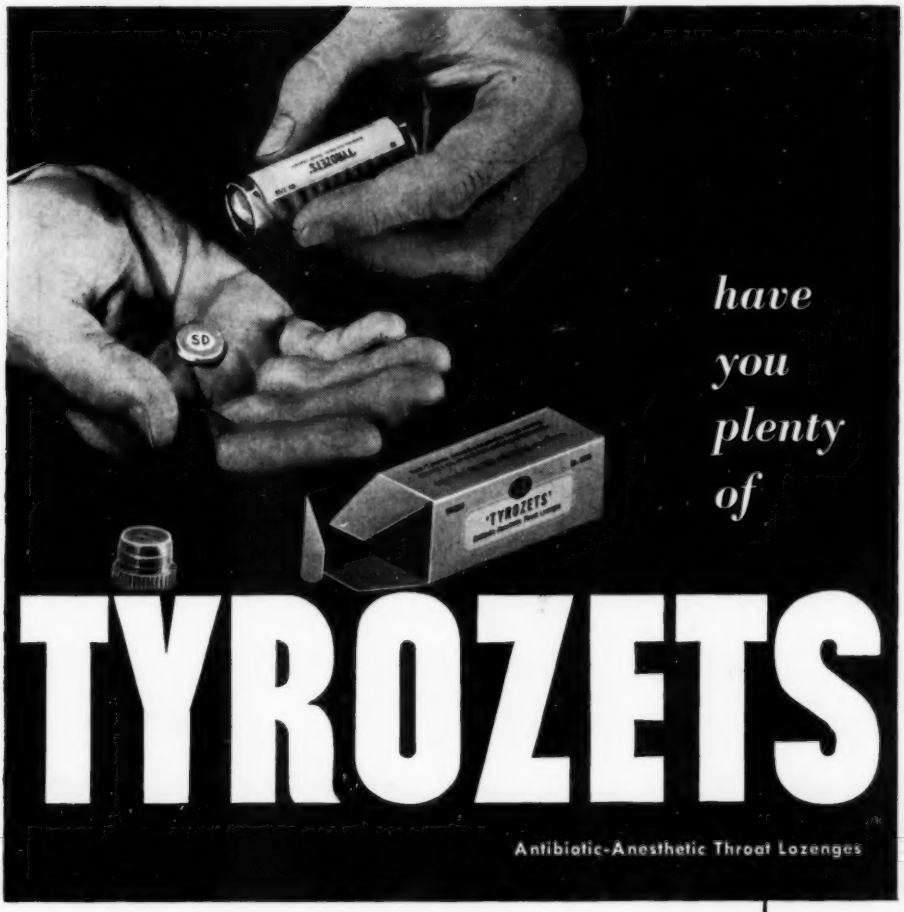

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